Evaluating the reward-enhancing effects of nicotine on ethanol self-administration in male and female rats

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Abstract: Nicotine and alcohol dependence disorders are highly correlated: Up to 80% of alcohol-dependent persons in the US smoke regularly, and alcohol dependence is four times more prevalent among people who are nicotine-dependent. There is mounting evidence that the reward-enhancing properties of nicotine synergistically enhance behavior directed at obtaining other rewards. To investigate the role of reward enhancement by nicotine in the comorbidity of nicotine- and alcohol-abuse, we measured the impact of nicotine exposure on rats' willingness to expend effort to self-administer alcohol. Because men and women differ in their responses to alcohol, we studied both male and female rats, and compared the results obtained with the two sexes.

Presentation Title: Evaluating the reward-enhancing effects of nicotine on ethanol self-administration in male and female rats
Program#/Poster#: 50.06/F21
Time: Saturday, Oct. 17, 1:00 PM – 5:00 PM
Location: Hall A

Fluoxetine potentiates methylphenidate-induced behavioral stereotypies and subsequent cocaine self-administration in rats

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Abstract: The stimulant drug methylphenidate (Ritalin) is used to treat attention-deficit hyperactivity disorder (ADHD) and is often abused by students as a cognitive enhancer. Like cocaine, methylphenidate works by blocking the reuptake of dopamine in the brain; but unlike cocaine, it does not affect serotonin, which may explain methylphenidate's comparatively reduced addiction risk in most people. We found that adding fluoxetine (a selective serotonin reuptake inhibitor or SSRI) to methylphenidate caused an increase in cocaine-like repetitive behavior (stereotypies) in subpopulation of adult rats that also self-administered cocaine in later phase. Our findings suggest that SSRIs may enhance the risk of addiction to methylphenidate in vulnerable individuals.

Presentation Title: Fluoxetine potentiates methylphenidate-induced behavioral stereotypies and subsequent cocaine self-administration in rats
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Location: Hall A

Deep brain stimulation (DBS) of nucleus accumbens afferent structures attenuates the reinstatement of cocaine seeking

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Abstract: Cocaine abuse is a major public health concern, with more than million current users in the United States alone. One of the major obstacles in treating cocaine addiction is the discouragingly high rate of relapse after detoxification. Previous work has shown that deep-brain stimulation (DBS) of the nucleus accumbens shell reduced cue-induced relapse to cocaine-seeking in rats. In this study we found that DBS applied to areas closely linked to the nucleus accumbens—the medial prefrontal cortex, ventral hippocampus, and basolateral amygdala—also reduced the reinstatement of cocaine seeking. These results suggest a promising role for DBS as a possible therapeutic tool for treating cocaine addiction and reducing the risk of relapse.

Presentation Title: Deep brain stimulation (DBS) of nucleus accumbens afferent structures attenuates the reinstatement of cocaine seeking
Program#/Poster#: 51.16/G8
Time: Saturday, Oct. 17, 1:00 PM – 5:00 PM
Location: Hall A

Pharmacological antagonism of the toll-like receptor 4 attenuates cocaine induced reinstatement

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Abstract: Researchers have hypothesized that cocaine triggers inflammation in the brain, which contributes to users' vulnerability to relapse. We showed that, consistent with this hypothesis, rats that self-administered cocaine exhibited increased levels of key inflammation-promoting protein, interleukin-1 beta (IL-1β), in the brain. Moreover, treating the animals with a compound that prevented this increase reduced their motivation to resume self-administering the drug.

Presentation Title: Pharmacological antagonism of the toll-like receptor 4 attenuates cocaine induced reinstatement
Program#/Poster#: 51.24/G16
Time: Saturday, Oct. 17, 1:00 PM – 5:00 PM
Location: Hall A

Identification of distinct neuronal ensembles selectively activated by discrete cues associated with cocaine or heroin seeking in rats

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Abstract: Learned associations between drug-related cues (or contexts) and the rewarding effects of the drug are thought to be encoded by sparsely distributed but interconnected groups of neurons called *neuronal ensembles*. Here, we sought to determine whether the neuronal ensembles encoding cocaine- and heroin-related cues are overlapping or distinct in the brains of rats. The animals were trained to self-administer cocaine and heroin on alternate days, each drug paired with distinct cues; then, using RNAscope assay, a method able to detect specific neural activity in the dorsal and ventral medial prefrontal cortex, we found that the neuronal ensembles encoding cue-related memories linked to the two drugs were distinct.

Presentation Title: Identification of distinct neuronal ensembles selectively activated by discrete cues associated with cocaine or heroin seeking in rats
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Time: Saturday, Oct. 17, 1:00 PM – 5:00 PM
Location: Hall A

Remembering to abstain: The impact of working memory on length of first quit attempt in drug users

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Abstract: Drug addiction continues to be a major public health problem: More than 20 million Americans aged 12 or older use illicit drugs. While much attention is given to treatment and prevention, limited attention is given to drug users' own efforts to quit. One factor associated with the difficulty they have quitting may be related to poorer working memory in this group. In a sample of 16 drug-using adults in Baltimore, Maryland, we found that those with stronger working memory ability achieved longer period of nonuse during quit attempts. These findings suggest that exercises to improve working memory in individuals who are struggling to maintain abstinence may help their treatment be more successful.

Presentation Title: Remembering to abstain: The impact of working memory on length of first quit attempt in drug users
Program#/Poster#: 52.08/G27
Time: Saturday, Oct. 17, 1:00 PM – 5:00 PM
Location: Hall A

Nicotine attenuates the effects of HIV-1 proteins on the neural circuitry of working and contextual memory

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Abstract: HIV infection can cause neurocognitive disorders due to synaptic damage and loss of neurons in the brain. Nicotine has been found to act as a cognitive enhancer in some individuals with neurocognitive problems, but whether it has any beneficial effects on memory and ability to make new synaptic connections in people with HIV-related neurocognitive disorders is unknown. In this study, we found that chronic nicotine treatment significantly lessened spatial and emotional memory deficits in HIV-infected rats. It also reversed the effects of the HIV-1 proteins o the expression of genes involved in synaptic plasticity in several key brain areas that mediate the processing of memory and emotion. Our findings indicate that nicotine can reduce the damaging effects of HIV on some aspects of memory and learning.

Presentation Title: Nicotine attenuates the effects of HIV-1 proteins o the neural circuitry of working and contextual memory
Program#/Poster#: 52.13/G32
Time: Saturday, Oct. 17, 1:00 PM – 5:00 PM
Location: Hall A

Partial inhibition of monoamine oxidase (MAO) increases nicotine self-administration in rats

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Abstract: Monoamine oxidase (MAO), an enzyme that breaks down certain neurotransmitters and moderates their effects, is inhibited in the brains of chronic cigarette smokers by approximately 40%; previous research has found that this may enhance people's response to nicotine, especially at low nicotine doses. We examined the effects of various doses of an MAO inhibitor called tranylcypromine (TCP) on nicotine self-administration in adult rats; self-administration of nicotine was directly related to the amount of MAO inhibition, and in the range of partial MAO inhibition seen in cigarette smokers, MAO inhibition increased rats' responding for nicotine. These data may be important for the FDA as they consider a mandated reduction in the nicotine content of combustible products; our findings suggest that cigarette constituents that inhibit MAO are likely to shift the reinforcing value of low-nicotine products.

Presentation Title: Partial inhibition of monoamine oxidase (MAO) increases nicotine self-administration in rats
Program#/Poster#: 143.02/I9
Time: Sunday, Oct. 18 8:00 AM – 12:00 PM
Location: Hall A

Nicotine self-administration is enhanced in obesity-resistant rats

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Abstract: Cigarette smoking and obesity are two major challenges to public health. Smokers with higher body mass index (BMI) smoke more cigarettes per day and may be more nicotine dependent than lean smokers. However, very little is understood about the relationship between obesity and nicotine reinforcement and whether obese smokers may respond differently to nicotine reduction in cigarettes—which the FDA is considering mandating. We studied nicotine self-administration in three groups of rats—a group made obese with a high-caloric diet, a group eating high-calorie food but resistant to obesity, and a control group. We found that nicotine self-administration, particularly at moderate and low doses, was enhanced in rats resistant to diet-induced obesity, suggesting that current lean smokers who eat densely caloric diet may continue to smoke at high rates following the reduction of nicotine in cigarettes, prolonging their exposure to the harmful chemicals in cigarette smoke.

Presentation Title: Nicotine self-administration is enhanced in obesity-resistant rats
Program#/Poster#: 143.06/I13
Time: Sunday, Oct. 18, 8:00 AM – 12:00 PM
Location: Hall A

Effects of central and peripheral oxytocin on reinstated cocaine seeking in male and femal rats

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Abstract: Because it affects natural and drug rewards via various brain pathways, oxytocin has gained increasing attention as a possible treatment for addiction. The oxytocin system is different in males and females, however: A greater number of oxytocin receptors are expressed throughout the addiction circuit in males than in females, but the underlying neurobiology and potential addiction therapies have typically only been studied in males. In a rat model of relapse to cocaine seeking, we found males and females both showed reduced cocaine seeking and reduced responding to cocaine cues i they received oxytocin. Oxytocin impacted reinstated cocaine seeking similarly in both sexes.

Presentation Title: Effects of central and peripheral oxytocin on reinstated cocaine seeking in male and female rats
Program#/Poster#: 144.08/I45
Session Time: Sunday, Oct. 18, 8:00 AM – 12:00 PM
Location: Hall A

Pathological persistence of the brain response to "unseen" 33 msec cocaine cues as a marker of relapse vulnerability

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Abstract: sensitive predictor of patients' vulnerability to cocaine relapse will be useful for identifying optimal treatment intensity, as well as for screening potential anti-relapse medications. We measured the reactivity of brain circuitry that mediates motivation in treatment-seeking patients' while repeatedly exposing them to subliminal cocaine-related cues in a protocol designed to delink the cues from their associations with the drug. Those patients whose circuitry remained highly reactive to the cues despite encountering them many times without any drug reinforcement relapsed at higher rates.

Presentation Title: Pathological persistence of the brain response to "unseen" 3 msec cocaine cues as a marker of relapse vulnerability
Program#/Poster#: 144.10/I47
Time: Sunday, Oct. 18, 8:00 AM – 12:00 PM
Location: Hall A

Innate immune molecules protect synapses from excess microglia-mediated pruning during CNS development

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Abstract: Microglia, the brain's resident immune cells, are emerging as critical regulators of healthy brain development. Recent studies from our lab and others indicate that microglia are responsible for pruning unused synapses during development; however, how microglia know which specific synapses to target for removal remains a major open question. We found that molecules that play role in the brain's immune responses against dead cells or debris appear to play a role in directing microglial pruning activities and have identified an immune protective signal that prevents microglia from targeting needed synapses. Refinement of synapses by microglia thus appears to depend on a careful balance of regulating signals. Understanding the consequences of disrupting this balance may provide insight into disorders characterized by immune dysregulation and brain circuit abnormalities.

Presentation Title: Innate immune molecules protect synapses from excess microglia-mediated pruning during CNS development
Topic: ++B.08.i. Other
Time: Sunday, Oct. 18, 9:00 AM - 9:15 AM
Location: S404

The effects of smoking reduced nicotine cigarettes upon resting state functional connectivity, craving and withdrawal in young smokers

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Abstract: Smoking contributes to more than 540,000 premature deaths each year in the United States, and a policy to reduce nicotine content is viewed as a way to reduce cigarette use. This study examined whether the nicotine yield of a cigarette affects brain and behavioral responses to smoking. fMRI scans of smokers revealed that positive coupling between the default mode network and both the salience network and executive control network was reduced after smoking, with greater reduction after smoking the participants' preferred brand than after smoking a reduced-nicotine cigarette. Smoking also enhanced sustained attention, especially when smoking higher-nicotine cigarettes. However, smoking reduced cigarette craving and withdrawal, irrespective of the type of cigarette smoked or the nicotine yield. The results suggest that reduced-nicotine cigarettes may still reduce craving and withdrawal while impacting brain activity and attention to a lesser degree than standard cigarettes.

Presentation Title: The effects of smoking reduced nicotine cigarettes upon resting state functional connectivity, craving and withdrawal in young smokers
Program#/Poster# 313.01/I26
Time: Monday, Oct. 19, 8:00 AM – 12:00 PM
Location: Hall A

A history of physical, emotional, or sexual abuse predicts higher mesolimbic response to drug cues in cocaine-dependent patients

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Abstract: Previous studies have reported that a history of adverse life experiences is associated with higher rates of mental health issues, including addiction. Here, we investigated whether a history of physical, emotional, or sexual abuse in cocaine-dependent patients was associated with greater activity in brain reward circuits in response to cocaine cues. group of cocaine-dependent patients were shown cocaine cues and neutral cues while being scanned in an MRI. As predicted, we found that patients who had previously reported experiencing emotional, physical, or sexual abuse had greater brain activation to the cocaine (vs. neutral) cues in several parts of the reward circuit, including the ventral tegmental area, ventral striatum, dorsal striatum, and caudal orbitofrontal cortex. These results provide initial evidence that a history of abuse could have an impact on brain activity that drives drug seeking and suggest the need for treatment that is individually tailored based on patients' abuse history, if any.

Presentation Title: history of physical, emotional, or sexual abuse predicts higher mesolimbic response to drug cues in cocaine-dependent patients
Program#/Poster#: 315.05/J15
Time: Monday, Oct. 19, 8:00 AM – 12:00 PM
Location: Hall A

The novel dopamine D3 receptor antagonists CAB02-015 and BAK4-54 inhibit oxycodone self-administration and reinstatement of drug-seeking behavior in rats

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Abstract: The misuse of prescription opioid pain relievers like oxycodone, as well as overdose deaths from these drugs, has increased dramatically in recent years. Thus, understanding their rewarding properties and developing effective medications to treat prescription opioid addiction has become a critical matter of public health. We studied the potential roles of two compounds, CAB02-015 and BAK4-54, in lessening oxycodone's rewarding effects in rats; these compounds act as antagonists, blocking the ability of opioids to interact with the dopamine D3 receptor. Treating rats with either of these compounds inhibited their self-administration of oxycodone; CAB02-015 was also found to speed the extinction of drug-seeking behavior and inhibit relapse. Thus, these novel D3 antagonists may have therapeutic potential for treatment of prescription opioid addiction.

Presentation Title: The novel dopamine D3 receptor antagonists CAB02-015 and BAK4-54 inhibit oxycodone self-administration and reinstatement of drug-seeking behavior in rats
Program#/Poster#: 319.01/K42
Time: Monday, Oct. 19, 8:00 AM – 12:00 PM
Location: Hall A

Chronic intermittent pattern of alcohol use promotes degradation of HDAC4 and HDAC5 in the rat striatum and enhances compulsive cocaine self-administration

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Abstract: Cocaine addiction is invariably preceded by experiences with legal and decriminalized drugs such as alcohol, nicotine, and marijuana, but the biological mechanisms by which prior drug experiences contribute to the development of cocaine addiction are poorly understood. We found that prior alcohol exposure in rodents enhances the effects of cocaine by inhibiting the activity of an enzyme called nuclear histone deacetylase (HDAC) in the striatum, a brain region critical for addiction-related reward, and that this involves a gene known to play a role in the transition from recreational to habitual cocaine use. Our findings show that intermittent alcohol consumption enhances vulnerability to cocaine addiction and gives new insight into the mechanisms that account for this.

Presentation Title: Chronic intermittent pattern of alcohol use promotes degradation of HDAC4 and HDAC5 in the rat striatum and enhances compulsive cocaine self-administration
Program#/Poster#: 411.01/L1
Time: Monday, Oct. 19, 1:00 PM – 5:00 PM
Location: Hall A

An allosteric modulator of the mu-opioid receptor promotes opioid-mediated antinociception

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Abstract: Positive allosteric modulators of the mu-opioid receptor (mu-PAMs) are compounds that bind to a site on the receptor that is distinct from the site used by endogenous opioids (endorphins) and traditional opioid analgesics; they are thus able to alter or enhance the activity of those molecules. We found that a mu-PAM called BMS-98612 caused a substantial increase in the pain-blocking activity of methadone and a moderate increase in the pain-blocking activity of morphine. At higher doses, this compound was able to briefly block pain signaling by itself. These and other findings demonstrate that mu-PAMs enhance the pain-blocking activity of opioid drugs, which would potentially enable them to be given at a lower dose – reducing risk of overdose and addiction.

Presentation Title: An allosteric modulator of the mu-opioid receptor promotes opioid-mediated antinociception
Program#/Poster#: 514.09/P22
Time: Tuesday, Oct. 20, 8:00 AM – 12:00 PM
Location: Hall A

The effects of N-Acetylcysteine on corticostriatal resting-state functional connectivity mediate nicotine withdrawal symptoms and may help prevent relapse

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Abstract: Chronic exposure to drugs of abuse disrupts brain circuits in the cortex and striatum that involve the neurotransmitter glutamate, and this in turn leads to drug seeking. In animals, a medication called N-acetylcysteine has been found to prevent relapse to drug seeking by normalizing glutamate transmission in some brain areas, but its effects in humans is unknown. We examined the effects of N-Acetylcysteine on cortical and striatal connectivity, nicotine withdrawal symptoms, and ability to maintain abstinence in a group of adult smokers receiving monetary incentives to help them quit. As compared to placebo, smokers receiving N-Acetylcysteine maintained abstinence more often, reported less craving and better mood, and showed more normalized cortical and striatal connectivity, indicating that this compound may help restructure reward processing and reduce vulnerability to relapse after quitting smoking.

Presentation Title: The effects of N-Acetylcysteine on corticostriatal resting-state functional connectivity mediate nicotine withdrawal symptoms and may help prevent relapse
Program#/Poster#: 780.09/J7
Time: Wednesday, Oct. 21, 1:00 PM – 5:00 PM
Location: Hall A